Locus	aGvHD Risk	#A	#P	HR Range	p Value Range	DSS Range	DSS Mean
A*	Low	11	389	0.64-1.57	0.2-0.8	1.04-5.66	2.62
	High	4	214	1.78-3.45	<0.001-0.003	1.04-4.3	2.39
B*	Low	4	200	1.28-1.48	0.118-0.538	1.74-2.81	2.53
	High	2	30	3-3.34	<0.001-0.015	1.06-1.06	1.06
Cw*	Low	18	578	0.46-2.88	0.057-0.899	1.52-23.9	15.1
	High	17	600	1.67-6.22	0.001-0.043	1.52-23.86	15.97
DRB1*	Low	25	729	0.47-2.25	0.079-0.985	1.3-13.33	4.91
	High	2	76	2.13-3.19	<0.001-0.003	4.02-10.41	7.22
DQB1*	Low	24	900	0.57-1.58	0.062-0.98	0.24-20.61	10.37
	High	3	114	1.75-2.81	0.002-0.017	1.38-20.61	13.74

combinations are 13.88 and 15.33, respectively. The following table summarizes DSS means and ranges for high and low risk combinations.

(Table 1) #A: # of allele combinations analyzed by Histocheck

#P: # of donor/patient pairs that have all the analyzed combinations

HR: Hazard Ratios of developing severe aGvHD

P values: for the corresponding estimated hazard risk

Conclusion: Our analysis demonstrates that means and ranges of DSS were interchangeable among high and low risk allele combinations within loci A, B, and Cw. In loci DRB1 and DQB1 DSS means were higher in the high risk combinations but the ranges remain overlapping. This analysis does not support selecting donors for HSCT recipients on the basis of low HistoCheck scores.

IMMUNE RECONSTITUTION

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CYTOTOXIC T LYMPHOCYTES (CTL) SPECIFIC FOR CMV, ADENOVIRUS, AND EBV CAN BE GENERATED FROM NAIVE T CELLS FOR ADOPTIVE IMMUNOTHERAPY

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Adoptive immunotherapy with peripheral blood (PB)-derived CMV/Ad/EBV-specific CTL generated from seropositive donors effectively prevents viral disease after Peripheral Blood Stem Cell Transplant (PBSCT), but this option has not been feasible when the donor T-cells are naive. PBSCT from CMV-seronegative (CMVneg) donors to CMV-seropositive (CMVpos) recipients produces a high incidence of CMV infection since donor T-cells are naïve to this virus. Umbilical cord blood (CB) is an important source of stem cells for allotransplant patients lacking human leukocyte antigen (HLA)-matched donors. T-cells in CB grafts are, however, also virus-naïve, leading to higher infections rates with CMV, EBV, adenovirus (Ad) and other viruses. Irrespective of whether the naive T-cells are sourced from CB or CMVneg PB, CTL generation for clinical use from these donors has been unsuccessful. We have now overcome this problem and can routinely generate CMV, Ad and EBV specific CTL from CB and CMV-specific CTLs from seronegative PB **for clinical use**. We used an Ad5f35CMVpp65 vector to transduce CB or PB derived dendritic cells and stimulated virus-specific CTL in the presence of IL-7, IL-12 and IL-15. This was followed by 2 stimulations with autologous EBV-lymphoblastoid cell lines (LCL) transduced with the same vector. CB-derived CTL were predominantly CD8+ (mean 87%;range 81-94) and had significant cytotoxicity against CMVpp65, Adhexon/penton and LCL targets. In addition, we generated CMVpp65, Adhexon/penton and LCL-specific responses from the PB of 4 CMVneg adult donors, which produced a mean of 92 (range 50-126), 163 (range 69-293), and 62 (range 37-86) SFC to CMVpp65 respectively. Neither CB nor CMVneg-derived CTL responded to irrelevant peptides. Of note, the virus-specific T-cells expanded from CB and CMVneg donors derived only from T-cells with a naive phenotype (CD45RA+/CCR7+). Moreover, both CB and CMVneg-derived CTL recognized "unconventional" CMVpp65 epitopes, as identified by overlapping pp65 peptide pools and confirmed by IFN-γ ELISPOT as well as multimer analysis. In HLA-A2+ subjects, naive-derived CTL did not recognize conventional HLA-A2 associated CMV pp65 epitopes such as NLV, suggesting an inherent difference between naïve and memory T-cell responses to CMV. In summary, virus-specific responses T-cell responses can be obtained even from CB and virus-naive adult donors and may allow prevention and treatment of viral disease in the recipients of these allografts.

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DENDRITIC CELL FACILITATE THYMIC RECOVERY AND ENHANCE IMMUNE RECONSTITUTION AFTER HEMATOPOIETIC STEM CELL TRANSPLANT

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After hematopoietic stem cell transplantation (HSCT), the first committed cells to engraft in the thymus are dendritic cells (DCs). The role of thymic DCs in T cell production by ensuring efficient tolerance and selection has been well demonstrated, however the role of thymic DCs in facilitating donor engraftment has not been investigated. Here we show addition of ex-vivo generated DCs accelerates thymic engraftment as well as enhance T cell recovery after HSCT. Control group received 10^3 $lin^-sca\text{-}1^+c\text{-}kit^+$ (LSK) (CD45.2) hematopoietic stem cell progenitors while the DCs group received 10^3 LSK (CD45.2) cells along with 10^3 ex-vivo generated DCs. DCs were generated using bone marrow from GFP^+ CD57/Bl mice (CD45.1/GFP^+) and cultured for 7 days with GMCSF. On the day of HSCT, C57/BL (CD45.1) recipients received lethal radiation at 1000 cGy. At 4 and 7 days after HSCT, thymuses of the DCs group had GFP^+ $CD11c^+$ cells present in the medullary region confirmed by immunohistochemistry and contained 1.8 and 4.2- fold, respectively, higher number of thymocytes compared to control group ($p < 0.05$). Furthermore, thymuses of the DCs group showed a 3.2 and 7.4-fold, respectively, higher number of thymoctyes derived from donor LSK (CD45.2) cells compared to the control group ($p < 0.05$ and $p < 0.007$). Two and four weeks after HSCT, peripheral blood of DCs group contained at least 2.6 and 4.8-fold, respectively, higher numbers of $CD3^+$ cells derived from donor LSK (CD45.2) cells compared to the control group ($p < 0.05$). Here, we demonstrate that ex-vivo generated DCs efficiently migrate and home to the thymic medulla and hasten thymic recovery as demonstrated by the higher number of total thymoctyes. Furthermore, DCs facilitate thymic engraftment as shown by increase number of donor thymoctyes. Lastly, recipients of DCs have earlier generation of de-novo donor derived $CD3^+$ T cells in the peripheral blood. By using the GFP^+ (CD45.1) cells along with donor LSK (CD45.2), we were able to confirm that the facilitation of early thymic recovery was due to the increased engraftment of the donor cells rather than autologous recovery of the host. Thus, this study suggests that DCs committed prior to thymic entry maintains the ability to home to the medullary region and facilitate thymoctye recover and hasten immune reconstitution after HSCT.

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CD40-ACTIVATED B CELLS MIGRATE TOWARDS SECONDARY LYMPHOID ORGANS AND INTERACT DYNAMICALLY WITH T CELLS

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B cells have been demonstrated to present antigen to T cells in vivo. CD40-activation dramatically improves antigen presentation by normal and malignant B cells and has therefore been studied as an approach to generate autologous "non-artificial" antigen presenting cells for active immunotherapy. Furthermore, CD40-B cells have recently been shown to expand tumorantigen and viral specific CTL